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Atrioventricular Delays, Cardiac Output and Diastolic Function in Patients with Implanted Dual Chamber Pacing and Sensing Pacemakers

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Abstract: The Cardiac Output (CO), Filling Time (FT) and Myocardial Performance Index (MPI) derived optimal atrioventricular delay (AVD), were compared and systolic and diastolic performance at every optimal AVD were analyzed. Thirty-two patients with implanted DDD pacemaker were investigated from implantation time to 6 months following PM implantation, in Cardiovascular Research Center of Tabriz University of Medical Sciences. The evaluation was performed during AV sequential pacing with different programmed AVDS ranged from 100 to 200 msec by steps of 20-30 msec. At every AVD, the following parameters were measured: FT, mitral VTI, ET, aortic VTI, ICT and IRT. CO and FT derived optimal AVDs were significantly different (146±37 and 126±35 msec, respectively), but their difference with MPI derived optimal AVDs was not significant (130±28 msec). ICT/ET was similar at CO, FT and MPI derived optimal AVD (0.24±0.10, 0.22±0.05 and 0.20±0.07, respectively). IRT/ET ratio was similar at CO, FT and MPI derived optimal AVDs (0.46±0.14, 0.45±0.10 and 0.42±0.10, respectively). Different methods indicate different optimal AVDs. However analysis of systolic and diastolic performance shows that different AVDs result in similar systolic or diastolic performance. At MPI optimized AVD, a high CO combined with the most advantageous conditions of both isovolumic contraction and relaxation phases is achieved.

Key words: Atrioventricular delay, cardiac output, pacemaker, implant

INTRODUCTION

In patients receiving a (Dual chamber pacing and sensing with inhibition and tracking) pacemaker (PM), atrioventricular interval (AVI) is a critical parameter to increase hemodynamics since an appropriately timed atrial systole can improve left ventricular filling and stroke volume according to the Frank-Starling law. Optimization of this interval is critical in patients to obtain hemodynamic benefit from the pacemaker (Styliadis *et al*., 2006).

Pacemaker programming with the periodic echocardiographic evaluation of the optimal AVI, pacing rate and mode is imperative for optimal results (Topilski *et al*., 2006). The efficacy of short atrioventricular (AV) delay in patients with severe cardiac hypofunction has been reported by Ishikawa *et al*. (2000). Cannon waves may be induced by programming excessively short AV intervals and diastolic mitral regurgitation may occur with excessively long programmed AV intervals. The AV interval is considered optimal (AV_{opt}) if it allows maximum cardiac output (Melzer *et al*., 2004). The duration of the optimal AV interval varies throughout a wide range among individuals, primarily the result of appreciable differences in interatrial conduction (Melzer *et al*., 2004).

Atrioventricular delay (AVD) is critical in patients with DDD pacemakers. Echo/Doppler evaluation of AVD providing the longest left ventricular filling time Cardiac Output (CO) is used for AVD optimization. Myocardial Performance Index (MPI) has been shown to improve by optimizing AVD (Porciani *et al*., 2004). So, optimization of AVD significantly contributes to maximum cardiac performance (Melzer *et al*., 2004; Meluzín *et al*., 2004; Maurer *et al*., 2003; Ishikawa *et al*., 1999a). Improvement of cardiac function has been reported in patients with severely reduced cardiac function, by implanting DDD pacemaker and setting a short AV delay (Ishikawa *et al*., 1999a, 2000).

This study was aimed to compare the Cardiac Output (CO), Filling Time (FT) and Myocardial Performance Index (MPI) derived optimal atrioventricular delay (AVD) and to analyze systolic and diastolic performance at every optimal AVD.

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MATERIALS AND METHODS

This is a descriptive, cross sectional study, performed on patients underwent DDD pace maker implantation from 2004 to 2005 in Cardiovascular Research Center of Tabriz Shahid Madani Hospital, including the patients presenting for the day after analysis or the patients presenting for follow up during 6 months following PM implantation.

Thirty two patients (19 men and 13 women), aged 66±17 years, mean ejection fraction 43%, with a DDD PM for sick sinus syndrome, CHB, or AV block Mobitz II, underwent echo/Doppler AVD optimization. Atrial leads were inserted in RA appendage and ventricular leads were implanted in RV apex. Concurrent with PM-analysis, Doppler and two-dimensional (2D) echocardiography was performed by commercially available instrument, VIVID-GE-Norway-7 echocardiograph. Indications for PM implantation and associated conditions were recorded for each patient. Patients with severe VHD and those with HR higher than pacing rate were excluded from the study.

Echocardiography in parasternal long axis view, for measuring LVOT (left ventricular outflow tract) diameter with optimal zooming, was performed on aortic valve. This diameter was used for calculation of LVOT cross section area as 2D×0.785. Using four chamber apical view with sample volume at the apex of mitral valve leaflets, we measured mitral E/A, VTI and FT. Aortic ET and VTI was measured by five chamber view with sample volume at LVOT. IVRT was measured by four chamber apical view with sample volume within LVOT and mitral valve. The heart rate (HR) was 60-120 beat/min and we programmed the pacing rate at least 10 beats higher than patient own HR, to assure that HR is stable during the study. Calculating of LVOT and EF, we analyzed PM and programmed AVD at range of 100 to 200 msec by steps of 20-30 msec (100,130,150,180 and 200 msec). At every AVD the following parameters was measured: FT, mitral VTI, ET, aortic VTI, ICT and IRT.

FT was calculated from beginning to end of mitral diastolic flow and followed with mitral VTI measurement. ET was calculated from beginning to end of aortic flow and followed with aortic VTI measurement. IVRT was calculated from end of aortic flow to beginning of mitral inflow. For calculation of IVCT, we used MCMO interval (the time between closing and opening of the mitral valve) and then IVCT = MCMO-(IVRT+ET) formula. All parameters were calculated in three consecutive cycles. CO was calculated by CO = SV×HR formula ($SV = 2\times D_{LVOT}\times 0.785\times VTI_{LVOT}$). For calculation of MPI we used this formula:

$$MPI = ICT+IRT/ET$$

Data entry and analysis were done by SPSS 11.5 software for windows. Continuous variables were expressed as mean±SD and analyzed using Student's t-test. Categorical variables were summarized as percentage and compared by chi-square analysis. p-values 0.05 considered as significant difference.

RESULTS

Of 32 studied patients 19 (59%) were male and 13 (41%) were female. The patients had the mean age of 66±17 years (range of 14 -84 year), mean LVEF of 43±13% (range of 15 to 66%) and mean HR of 84±12 beat/min (range of 60 to 115). The mean LVEF in male and female patients was 41 and 46%, respectively. The indication of DDD implantation was SSS in 9 (28%), CHB in 20 (62%), AV block Mobitz II in 1 (3.1%) and HOCM (hypertrophic obstructive cardiomyopathy) in 1 (3.1%). Five patients had MI (three antroseptal MI and two inferior MI). Mitral E/A in patients with DDD PM was <1 in 24 (75%), =1 in 5 (16%), >1 in 2 (6%) and >2 in 1 (3%).

Because of high HR and great difference of diastolic impairment in various AVDs, the assessment of mitral VTI and E/A in different AVDs was impossible.

CO and FT derived optimal AVDs were significantly different (146±37, 126±35 msec, respectively) (p = 0.01), but their difference with MPI derived optimal AVDs was not significant (130±28 msec) (p = 0.09). Optimal CO, MPI and FT derived ETs were 253±41, 257±42 and 253±41, respectively, with no significant difference. Optimal CO and MPI derived IRTs were not significantly different (114±28 and 108±25, respectively) (p = 0.08); also their difference with optimal FT derived optimal IRT was not significant (112±22) (p = 0.2). Optimal CO and MPI derived ICTs were significantly different (59±22 and 49±15, respectively) (P=0.01), but their difference with optimal FT derived optimal ICT was not significant (53±15) (p = 0.2).

ICT/ET was similar at CO, FT and MPI derived optimal AVD (0.24±0.10, 0.22±0.05 and 0.20±0.07, respectively). IRT/ET ratio was similar at CO, FT and MPI derived optimal AVDs (0.46±0.14, 0.45±0.10 and 0.42±0.10, respectively).

The patients were classified in two groups with EF = 50 and EF<50%. Then, the CO, MPI, FT, ICT/ET, IRT/ET and ET derived optimal AVDs were compared in two groups. The CO, MPI and FT derived optimal AVDs were not significantly different in two groups, but IRT/ET

Table 1: Comparison of optimal AVD in basis of various parameters in two group of EF<50% and EF≥50%

	EF (%)		
Optimal AVD	<50	50	p-value
CO	151	133	0.20
MPI	133	121	0.20
FT	121	137	0.20
IRT/ET in basis of CO	0.49	0.37	0.20
IRT/ET in basis of MPI	0.45	0.35	0.01
IRT/ET in basis of FT	0.47	0.38	0.03
ICT/ET in basis of CO	0.25	0.19	0.08
ICT/ET in basis of MPI	0.2	0.17	0.30
ICT/ET in basis of FT	0.2	0.19	0.30
ET in basis of CO	243	275	0.04
ET in basis of MPI	250	273	0.10
ET in basis of FT	242	277	0.20
IRT in basis of CO	119	101	0.09
IRT in basis of MPI	113	93	0.04
IRT in basis of FT	114	104	0.20
ICT in basis of CO	61	51	0.20
ICT in basis of MPI	50	45	0.40
ICT in basis of FT	53	52	0.90

in optimal CO, MPI and FT were significantly different in two groups. Also, ET in CO derived optimal AVD was significantly different in two groups (Table 1).

DISCUSSION

Atrial contraction and AV synchrony is important in CO increase. In normal cases atrial contraction institute approximately 20% of ventricular filling, but this is more critical in LVH or ventricular diastolic impairment, higher ages and tachycardia (Møller *et al*., 2000). Atrioventricular delay (AVD) is critical in patients with DDD pacemakers (PM), because it has good effect on atrial contractility, LV filling and stroke volume according the Starling low (Porciani *et al*., 2004).

Optimization of programmed atrioventricular delay in dual chamber pacing is essential to the hemodynamic efficiency of the heart. Automatic AV delay optimization in an implanted pacemaker is highly desirable. Variations of Peak Endocardial Acceleration (PEA) with AV delay at rest correlate well with echocardiography derived observations, particularly with end-diastolic filling and mitral valve closure timings. This suggests the possibility of devicing a procedure for the automatic determination of the optimal AV delay (OAVD) (Dupuis *et al*., 2003). In patients with an implanted DDD pacemaker (PM), the atrial contribution may be interrupted by too short an atrioventricular (AV) delay and filling time may be shortened by too long an AV delay. The AV delay at which the end of the A wave on transmitral flow coincides with complete closure of the mitral valve may be optimal (Ishikawa *et al*., 1999b). Ishikawa *et al*. (1999b) concluded that optimal AV delay can be predicted by this simple formula: slightly prolonged AV delay minus the interval between end of A wave and complete closure of mitral valve at the AV delay setting. The QT interval on the surface ECG is strongly influenced by the atrioventricular (AV) delay setting and changes in the QT interval are closely related to changes in cardiac function. In patients with implanted DDD pacemaker, cardiac output is maximal when atrioventricular (AV) delay is set to give the maximum QT interval (QTI) (Ishikawa *et al*., 2003). It has been reported recently that implanting a DDD pacemaker and setting a short AV delay in patients with severely reduced cardiac function leads to improved function (Ishikawa *et al*., 2003). The QT interval on the surface ECG is easily influenced by the AV delay setting and changes in the QT interval are closely related to changes in cardiac function (Ishikawa *et al*., 2001, 2002).

Topilski *et al*. (2006) studied 28 patients with hypertrophic obstructive cardiomyopathy (HOCM). In this study, a protocol using echocardiographic examination assessing the changes in the left ventricular outflow tract (LVOT) gradient in different atrioventricular intervals (AVIs), pacing rates and pacing modes was used for optimal pacemaker programming. Twenty-five patients with HOCM were implanted with DDD pacemakers and evaluated prospectively. The LVOT gradient was measured during periodic evaluations every 3 to 6 months. After each evaluation, the optimal AVI, pacing rate and mode were set on the basis of the minimal LVOT gradient not associated with systolic arterial cuff pressure reduction. During follow-up, the optimal AVI was prolonged in most patients. Sixty-four percent of patients showed a clear relation between pacemaker modifications and gradient reduction. In 75% of these patients, optimal gradient reduction required repeated AVI and pacing rate programming on the basis of echocardiographic evaluation. The symptomatic reduction was positively correlated with the LVOT gradient reduction. In conclusion, DDD pacing is effective in reducing the LVOT gradient and improving functional capacity in adult patients with hypertrophic cardiomyopathy. Pacemaker programming with the periodic echocardiographic evaluation of the optimal AVI, pacing rate and mode is imperative for optimal results (Topilski *et al*., 2006).

Kedia *et al*. (2006) evaluated the utility of atrioventricular (AV) optimization using Doppler echocardiography in patients who undergo cardiac resynchronization therapy (CRT). Five hundred patients underwent CRT, 215 of whom underwent AV optimization <30 days after implantation. AV delay was optimized using Doppler mitral inflow data to target stage I diastolic filling. The mean follow-up period was 23 months. Baseline and final AV delay means were 120 +/- 25 and 135 +/- 40 msec, respectively. In 40% of patients (86 of 215), final AV delay settings were >140 msec. There was no difference in mortality in patients with final AV delays of >140 msec. In conclusion, AV optimization in patients who underwent CRT resulted in final AV delay settings of >140 msec in 40% of patients. AV delay optimization based on Doppler echocardiographic determination of optimal diastolic filling is useful and safe in patients who undergo CRT (Kedia *et al*., 2006).

Atrioventricular (AV) delay optimization can be an important determinant of the response to cardiac resynchronization therapy (CRT) in patients with medically refractory heart failure and a ventricular conduction delay (Kerlan *et al*., 2006). In a study by Kerlan *et al*. (2006), 40 patients with severe heart failure, referred for CRT were studied using two-dimensional Doppler echocardiography. In each patient, the acute improvement in stroke volume with CRT in response to two methods of AV delay optimization was compared. The optimized AV delay determined by the aortic VTI method resulted in an increase in aortic VTI of 19±13% compared with an increase of 12±12% by the mitral inflow method. The optimized AV delay by the aortic VTI method was significantly longer than the optimized AV delay calculated from the mitral inflow method (119±34 msec versus 95±24 msec). So, AV delay optimization by Doppler echocardiography for patients with severe heart failure treated with a CRT device yields a greater systolic improvement when guided by the aortic VTI method compared with the mitral inflow method (Kerlan *et al*., 2006).

There was a significant positive correlation between the optimal AV delay at which CO was maximal (161±33 msec) and the optimal AV delay predicted from the maximum QT interval (167±29 msec) (Ishikawa *et al*., 1999a). Porciani *et al*. (2004) compared the CO, FT, MPI derived optimal AVD. Twenty-five patients with a DDD PM underwent echo/Doppler AVD optimization. CO, FT and MPI derived optimal AVDs were significantly different. ICT/ET was similar at CO, FT and MPI derived optimal AVD. IRT/ET ratio was similar at FT and MPI derived optimal AVDs and significantly shorter than at CO derived optimal AVD. Different methods indicate different optimal AVDs. However analysis of systolic and diastolic performance shows that different AVDs result in similar systolic or diastolic performance. At MPI optimized AVD, a high CO combined with the most advantageous conditions of both isovolumic contraction and relaxation phases is achieved (Porciani *et al*., 2004).

Porciani *et al*. (2006) studied 22 patients implanted with a biventricular device. The optimal AVD was identified by the minimum MPI. After optimization, the appropriate AVD was programmed in each patient. MPI at 6-month follow-up after optimization was significantly higher compared with baseline. Re-optimization of AVD significantly reduced MPI compared with the value prior to re-optimization. The MPI remained unchanged at 12-month compared with 6-month follow-up. Clinical sympto and reverse left ventricular remodeling were sustained at 6 and 12-month follow-up. It was concluded that optimal AVD changes over time in patients with heart failure. Sustained improvement in clinical sympto msec and reverse left ventricular remodeling after CRT are not temporally associated with improvement in MPI (Porciani *et al*., 2006).

Interatrial conduction blocks can be managed in some cases by proper programming of conventional DDD systems (Parravicini *et al*., 2000). Kubica *et al*. (1993) found statistically significant difference between stroke volume with various atrioventricular delays. During pacing rate of 70 ppm the maximal difference was 19 and 15% during 100 ppm. Comparing both pacing rates the distributions of hemodynamically optimal atrioventricular delays was also significantly different. The best atrioventricular delay from the hemodynamic point of view was 36 msec longer during 70 ppm of pacing rate than during 100 ppm. The most often optimal delay at 70 ppm was 190-200 msec and the rarest optimal delay was 90-100 msec; during 100 ppm pacing, respectively: 140-150 msec and 240-250 msec. There is considerable personal variability in the hemodynamic response for atrioventricular delay changing as well as in the hemodynamically optimal values of this parameter during both pacing rates. In conclusion: 1. Atrioventricular delay programming has significant influence on left ventricular stroke volume. 2. Programming of atrioventricular delay should be performed individually in every patient because of personal variability of optimal values of this parameter (Kubicia *et al*., 1993).

There were different optimal AVDs according CO, FT and MPI. Also, we concluded that Co derived optimal AVD is significantly higher than FT derived optimal AVD. So, what is the best method for optimization of AVD?

Analysis of parameters including IRT/ET and ICT/E as the components of MPI showed that there is not significant difference between CO, MPI and FT derived ICT/ET in optimal AVD. Also, the IRT/ET time in optimal AVD according the CO, MPI and FT is similar.

Because the main function of the heart is maintenance of sufficient CO for metabolic requirements of tissues, it see msec that determination of optimal AVD according the highest CO, to be the gold standard method. However, our findings showed that the optimal AVD according the highest CO makes the highest CO, but it dos not improve the diastolic function. Analysis of systolic intervals by using echo-Doppler showed that: (1) determination of Co derived optimal AVD is in basis of a long ET with a short ICT and a long IRT; (2) determination of FT derived optimal AVD is in basis of a short ET with a short ICT and a short IRT; (3) determination of MPI derived optimal AVD is in basis of a long ET with a short ICT and a short IRT.

CONCLUSION

Different methods indicate different optimal AVDs. However analysis of systolic and diastolic performance shows that different AVDs result in similar systolic or diastolic performance. At MPI optimized AVD, a high CO combined with the most advantageous conditions of both isovolumic contraction and relaxation phases is achieved. Regarding the importance of AV interval in CO of patients with implanted DDD PM, it is recommended that following DDD and also in patients with PM syndrome, PM analysis to be performed in combination with echocardiographic assessment.

REFERENCES

Dupuis, J.M., A. Kobeissi, L. Vitali, G. Gaggini and M. Merheb *et al*., 2003. Programming optimal atrioventricular delay in dual chamber pacing using peak endocardial acceleration: Comparison with a standard echocardiographic procedure. Pacing Clin. Elect., 26: 210-213.

Ishikawa, T., T. Sugano, S. Sumita, K. Kimura and M. Kikuchi, 1999a. Relationship between atrioventricular delay, QT interval and cardiac function in patients with implanted DDD pacemakers. Europace, 1: 192-196.

Ishikawa, T., S. Sumita, K. Kimura, M. Kikuchi and M. Kosuge, 1999b. Prediction of optimal atrioventricular delay in patients with implanted DDD pacemakers. Pacing Clin. Electrophysiol., 22: 1365-1371.

Ishikawa, T., S. Sumita, K. Kimura, M. Kikuchi and M. Kosuge *et al*., 2000. Efficacy of atrioventricular sequential pacing and diastolic mitral regurgitation in patients with intrinsic atrioventricular conduction. Jap. Circ. J., 64: 579-582.

Ishikawa, T., T. Suganao, S. Sumita, T. Nakagawa and M. Hanada *et al*., 2001. Optimal atrioventricular delay setting determined by evoked QT interval in patients with implanted stimulus-T-driven DDDR pacemakers. Europace, 3: 46-51.

Ishikawa, T., T. Sugano, S. Sumita, N. Toda and M. Kosuge *et al*., 2002. Optimal atrioventricular delay setting determined by QT sensor of implanted DDDR pacemaker. Pacing Clin. Electrophysiol., 25: 195-200.

Ishikawa, T., T. Sugano, S. Sumita, M. Kosuge and I. Kobayashi *et al*., 2003. Changes in evoked QT intervals according to variations in atrioventricular delay and cardiac function in patients with implanted QT-driven DDDR pacemakers. Circ J., 67: 515-518.

Kedia, N., K. Ng, C. Apperson-Hansen, C. Wang and P. Tchou *et al*., 2006. Usefulness of atrioventricular delay optimization using Doppler assessment of mitral inflow in patients undergoing cardiac resynchronization therapy. Am. J. Cardiol., 15: 780-785.

Kerlan, J.E., N.S. Sawhney, A.D. Waggoner, M.K. Chawla and S. Garhwal *et al*., 2006. Prospective comparison of echocardiographic atrioventricular delay optimization methods for cardiac resynchronization therapy. Heart Rhythm., 3: 148-154.

Kubica, J., G. Swiatecka, S. Sielski, L. Stolarczyk and G. Raczak, 1993. Left ventricular stroke volume in individuals with dual chamber pacemaker (DDD). Effect of atrioventricular delay. Kardiol. Pol., 39: 447-451.

Maurer, D.E., B. Naegeli, E. Straumann, O. Bertel and J. Frielingsdorf, 2003. Quality of life and exercise capacity in patients with prolonged PQ interval and dual chamber pacemakers: A randomized comparison of permanent ventricular stimulation vs intrinsic AV conduction. Europace, 5: 411-417.

Meluzín, J., M. Novák, J. Müllerová, J. Krejcí and P. Hude *et al*., 2004. A fast and simple echocardiographic method of determination of the optimal atrioventricular delay in patients after biventricular stimulation. Pacing Clin. Electrophysiol., 27: 58-64.

Melzer, C., A.C. Borges, F. Knebel, W.S. Richter and W. Combs *et al*., 2004. Echocardiographic AV-interval optimization in patients with reduced left ventricular function. Cardiovasc. Ultrasound, 2: 30-30.

Møller, J.E., S.H. Poulsen and K. Egstrup, 2000. Effect of preload alternations on a new Doppler echocardiographic index of combined systolic and diastolic performance. J. Am. Soc. Echocardiogr., 13: 644-644.

Parravicini, U., A. Mezzani, M. Bielli, T. Di Camillo and N.F. Pardo *et al*., 2000. DDD pacing and interatrial conduction block: Importance of optimal AV interval setting. Pacing Clin. Electrophysiol., 23: 1448-1450.

Porciani, M.C., G. Corbucci, F. Fantini, N. Musilli and A. Sabini *et al*., 2004. A perspective on atrioventricular delay optimization in patients with a dual chamber pacemaker. Pacing Clin. Electrophysiol., 27: 333-338.

Porciani, M.C., C. Dondina, R. Macioce, G. Demarchi and F. Cappelli *et al*., 2006. Temporal variation in optimal atrioventricular and interventricular delay during cardiac resynchronization therapy. J. Card Fail., 12: 715-719.

Styliadis, I.H., C.E. Papadopoulos, N.I. Gouzoumas, G. Giannakoulas and H.I. Karvounis *et al*., 2006. Similar pattern of diastolic function adaptation of both ventricles to programmed atrioventricular interval modification in patients with DDD pacing. Anadolu Kardiyol. Derg., 6: 243-247.

Topilski, I., J. Sherez, G. Keren and I. Copperman, 2006. Long-term effects of dual-chamber pacing with periodic echocardiographic evaluation of optimal atrioventricular delay in patients with hypertrophic cardiomyopathy >50 years of age. Am. J. Cardiol., 97: 1769-1775.